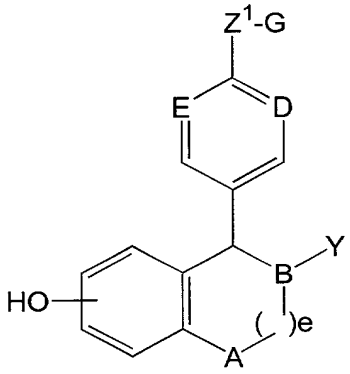
Claims:

1. A method for treating female sexual dysfunction comprising:

administering to a female subject in need thereof, an effective amount of an estrogen agonist / antagonist, and optionally,

co-administering an effective amount of a cyclic guanosine 3',5'-monophosphate elevator.

2. A method as in claim 1 wherein said estrogen agonist / antagonist of the following formula (I):




(I)

wherein:

A is selected from $CH_2$ and NR;

B, D and E are independently selected from CH and N;

Y is

(a) phenyl, optionally substituted with 1-3 substituents independently selected from $R^4$;

(b) naphthyl, optionally substituted with 1-3 substituents independently selected from $R^4$;

(c) $C_3$-$C_8$ cycloalkyl, optionally substituted with 1-2 substituents independently selected from $R^4$;

(d) $C_3$-$C_8$ cycloalkenyl, optionally substituted with 1-2 substituents independently selected from $R^4$;

(e) a five membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -$NR^2$- and -$S(O)_n$-, optionally substituted with 1-3 substituents independently selected from $R^4$;

(f) a six membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, $-NR^2-$ and $-S(O)_n-$ optionally substituted with 1-3 substituents independently selected from $R^4$; or

(g) a bicyclic ring system consisting of a five or six membered heterocyclic ring fused to a phenyl ring, said heterocyclic ring containing up to two heteroatoms selected from the group consisting of -O-, $-NR^2-$ and $-S(O)_n-$, optionally substituted with 1-3 substituents independently selected from $R^4$;

$Z^1$ is

(a) $-(CH_2)_p W(CH_2)_q-$;

(b) $-O(CH_2)_p CR^5R^6-$;

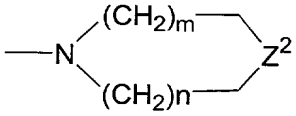
(c) $-O(CH_2)_pW(CH_2)_q-$;

(d) $-OCHR^2CHR^3-$; or

(e) $-SCHR^2CHR^3-$;

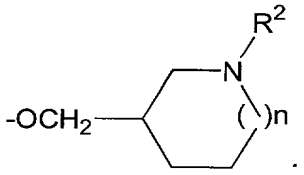
G is

(a) $-NR^7R^8$;

(b) 

wherein n is 0, 1 or 2; m is 1, 2 or 3; $Z^2$ is -NH-, -O-, -S-, or $-CH_2-$; optionally fused on adjacent carbon atoms with one or two phenyl rings and, optionally independently substituted on carbon with one to three substituents and, optionally, independently on nitrogen with a chemically suitable substituent selected from $R^4$; or

(c) a bicyclic amine containing five to twelve carbon atoms, either bridged or fused and optionally substituted with 1-3 substituents independently selected from $R^4$; or

$Z^1$ and G in combination may be  ;

W is

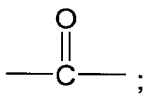
(a) $-CH_2-$;

(b) -CH=CH-;

(c) -O-;

(d) $-NR^2-$;

(e) $-S(O)_n-$;

(f)  ;

(g) $-CR^2(OH)-$;

(h) $-CONR^2-$;

(i) $-NR^2CO-$;

(j)  ; or

(k) $-C\equiv C-$;

R is hydrogen or $C_1$-$C_6$ alkyl;

$R^2$ and $R^3$ are independently

(a) hydrogen; or

(b) $C_1$-$C_4$ alkyl;

$R^4$ is

(a) hydrogen;

(b) halogen;

(c) $C_1$-$C_6$ alkyl;

(d) $C_1$-$C_4$ alkoxy;

(e) $C_1$-$C_4$ acyloxy;

(f) $C_1$-$C_4$ alkylthio;

(g) $C_1$-$C_4$ alkylsulfinyl;

(h) $C_1$-$C_4$ alkylsulfonyl;

(i) hydroxy ($C_1$-$C_4$)alkyl;

(j) aryl ($C_1$-$C_4$)alkyl;

(k) $-CO_2H$;

(l) -CN;

(m) -CONHOR;

(n) $-SO_2NHR$;

(o) $-NH_2$;

(p) $C_1$-$C_4$ alkylamino;

(q) $C_1$-$C_4$ dialkylamino;

(r) $-NHSO_2R$;

(s) $-NO_2$;

(t) -aryl; or

(u) -OH;

$R^5$ and $R^6$ are independently $C_1$-$C_8$ alkyl or together form a $C_3$-$C_{10}$ carbocyclic ring;

$R^7$ and $R^8$ are independently

(a) phenyl;

(b) a $C_3$-$C_{10}$ carbocyclic ring, saturated or unsaturated;

(c) a $C_3$-$C_{10}$ heterocyclic ring containing up to two heteroatoms, selected from -O-, -N- and -S-;

(d) H;

(e) $C_1$-$C_6$ alkyl; or

(f) form a 3 to 8 membered nitrogen containing ring with $R^5$ or $R^6$;

$R^7$ and $R^8$ in either linear or ring form may optionally be substituted with up to three substituents independently selected from $C_1$-$C_6$ alkyl, halogen, alkoxy, hydroxy and carboxy;

a ring formed by $R^7$ and $R^8$ may be optionally fused to a phenyl ring;

e is 0, 1 or 2;

m is 1, 2 or 3;

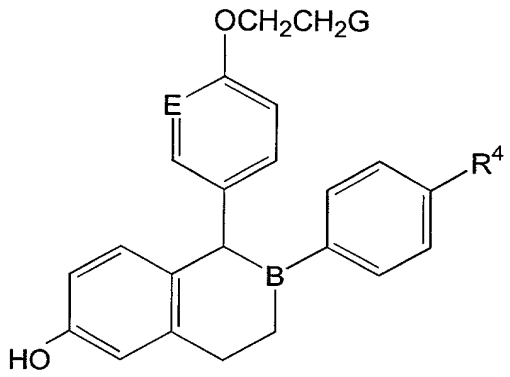
n is 0, 1 or 2;

p is 0, 1, 2 or 3;

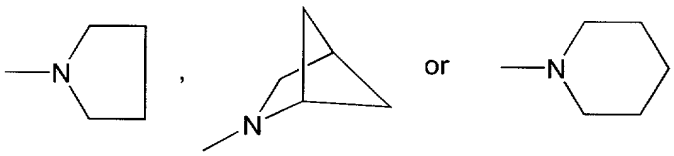
q is 0, 1, 2 or 3;

or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

3. A method as in claim 2 wherein said estrogen agonist / antagonist is a compound of formula (IA):




(IA)

wherein G is  ;

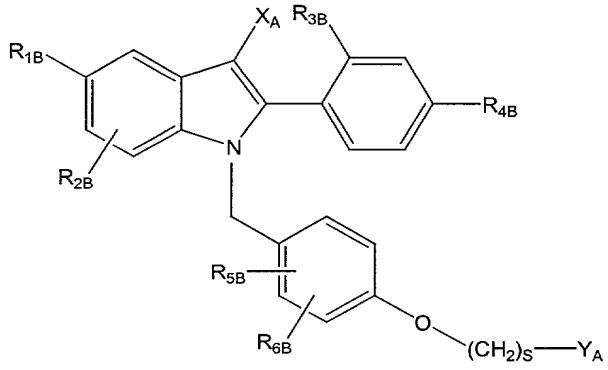
$R^4$ is H, OH, F, or Cl; and B and E are independently selected from CH and N or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof.

4. A method as in claim 3 wherein said estrogen agonist / antagonist is (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol or an optical or geometric isomer thereof; a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof.

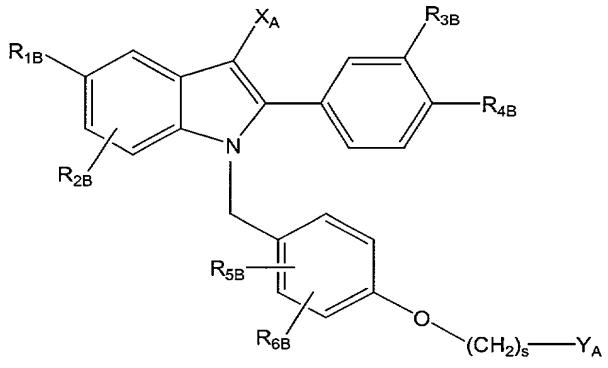
5. A method as in claim 4 wherein said estrogen agonist / antagonist is in the form of a D-tartrate salt.

6. A method as in claim 1 wherein said estrogen agonist / antagonist is selected from the group consisting of tamoxifen, 4-hydroxy tamoxifen, raloxifene, toremifene, centchroman, idoxifene, 6-(4-hydroxy-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-benzyl]-naphthalen-2-ol, {4-[2-(2-aza-bicyclo[2.2.1]hept-2-yl)-ethoxy]-phenyl}-[6-hydroxy-2-(4-hydroxy-phenyl)-benzo[b]thiophen-3-yl]-methanone, EM-652, EM-800, GW 5638, GW 7604, and optical or geometric isomers thereof; and pharmaceutically acceptable salts, N-oxides, esters, quaternary ammonium salts, and prodrugs thereof.

7. A method as in claim 1 wherein said estrogen agonist / antagonist is a compound selected from the formulas V or VI:




(V)




(VI)

wherein:

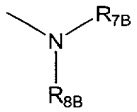
$R_{1B}$ is selected from H, OH, -O-C(O)-$C_1$-$C_{12}$ alkyl (straight chain or branched), -O-$C_1$-$C_{12}$ alkyl (straight chain or branched or cyclic), or halogens or $C_1$-$C_4$ halogenated ethers,

$R_{2B}$, $R_{3B}$, $R_{4B}$, $R_{5B}$, and $R_{6B}$ are independently selected from H, OH, -O-C(O)-$C_1$-$C_{12}$ (straight chain or branched), -O-$C_1$-$C_{12}$ (straight chain or branched or cyclic), halogens, or $C_1$-$C_4$ halogenated ethers, cyano, $C_1$-$C_6$ alkyl (straight chain or branched), or trifluoromethyl, with the proviso that, when $R_{1B}$ is H, $R_{2B}$ is not OH;

$X_A$ is selected from H, $C_1$-$C_6$ alkyl, cyano, nitro, triflouromethyl, and halogen;

s is 2 or 3;

$Y_A$ is the moiety:



wherein:

a) $R_{7B}$ and $R_{8B}$ are independently selected from the group of H, $C_1$-$C_6$ alkyl, or phenyl optionally substituted by CN, $C_1$-$C_6$ alkyl (straight chain or branched), $C_1$-$C_6$ alkoxy (straight chain or branched), halogen, -OH, $-CF_3$, or $-OCF_3$; or

b) $R_{7B}$ and $R_{8B}$ are concatenated to form a five-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, $C_1$-$C_4$ alkyl, trihalomethyl, $C_1$-$C_4$ alkoxy, trihalomethoxy, $C_1$-$C_4$ acyloxy, $C_1$-$C_4$ alkylthio, $C_1$-$C_4$ alkylsulfinyl, $C_1$-$C_4$ alkylsulfonyl, hydroxy ($C_1$-$C_4$)alkyl, $-CO_2H$, -CN, $-CONHR_{1B}$, $-NH_2$, $-NH(C_1$-$_{C4}$ alkyl), $-N(C_1$-$C_4$ alkyl$)_2$, $-NHSO_2R_{1B}$, $-NHCOR_{1B}$, $-NO_2$, or phenyl optionally substituted with 1-3 ($C_1$-$C_4$)alkyl; or

c) $R_{7B}$ and $R_{8B}$ are concatenated to form a six-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, $C_1$-$C_4$ alkyl, trihalomethyl, $C_1$-$C_4$ alkoxy, trihalomethoxy, $C_1$-$C_4$ acyloxy, $C_1$-$C_4$ alkylthio, $C_1$-$C_4$ alkylsulfinyl, $C_1$-$C_4$ alkylsulfonyl, hydroxy ($C_1$-$C_4$)alkyl, $-CO_2H$, -CN, $-CONHR_{1B}$, $-NH_2$, $-NH(C_1$-$C_4$ alkyl), $-N(C_1$-$C_4$ alkyl$)_2$, $-NHSO_2R_{1B}$, $-NHCOR_{1B}$, $-NO_2$, or phenyl optionally substituted with 1-3 ($C_1$-$C_4$)alkyl; or

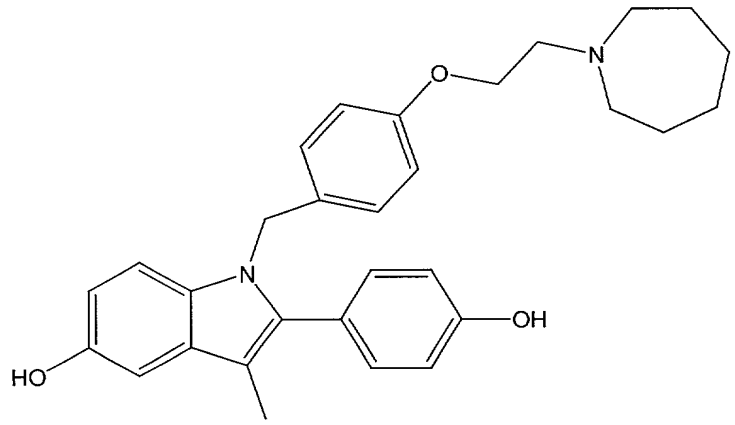
d) $R_{7B}$ and $R_{8B}$ are concatenated to form a seven-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, $C_1$-$C_4$ alkyl, trihalomethyl, $C_1$-$C_4$ alkoxy, trihalomethoxy, $C_1$-$C_4$ acyloxy, $C_1$-$C_4$ alkylthio, $C_1$-$C_4$ alkylsulfinyl, $C_1$-$C_4$ alkylsulfonyl, hydroxy ($C_1$-$C_4$)alkyl,

$-CO_2H$, -CN, $-CONHR_{1B}$, $-NH_2$, $-NH(C_1-C_4$ alkyl), $-N(C_1-C_4$ alkyl$)_2$, $-NHSO_2 R_{1B}$, $-NHCOR_{1B}$, $-NO_2$, or phenyl optionally substituted with 1-3 $(C_1-C_4)$alkyl; or

e) $R_{7B}$ and $R_{8B}$ are concatenated to form an eight-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, $C_1-C_4$ alkyl, trihalomethyl, $C_1-C_4$ alkoxy, trihalomethoxy, $C_1-C_4$ acyloxy, $C_1-C_4$ alkylthio, $C_1-C_4$ alkylsulfinyl, $C_1-C_4$ alkylsulfonyl, hydroxy $(C_1-C_4)$alkyl, $-CO_2H$, -CN, $-CONHR_1$, $-NH_2$, $-NH(C_1-C_4$ alkyl), $-N(C1-C4$ alkyl$)_2$, $-NHSO_2R_{1B}$, $-NHCOR_{1B}$, $-NO_2$, or phenyl optionally substituted with 1-3 $(C_1-C_4)$alkyl; or

f) $R_{7B}$ and $R_{8B}$ are concatenated to form a saturated bicyclic heterocycle containing from 6-12 carbon atoms either bridged or fused and containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, $C_1-C_4$ alkyl, trihalomethyl, $C_1-C_4$ alkoxy, trihalomethoxy, $C_1-C_4$ acyloxy, $C_1-C_4$ alkylthio, $C_1-C_4$ alkylsulfinyl, $C_1-C_4$ alkylsulfonyl, hydroxy $(C_1-C_4)$alkyl, $-CO_2H$, -CN, $-CONHR_{1B}$, $-NH_2$, $-NH(C_1-C_4$ alkyl), $-N(C_1-C_4$ alkyl$)_2$, $-NHSO_2R_{1B}$, $-NHCOR_{1B}$, $-NO_2$, or phenyl optionally substituted with 1-3 $(C_1-C_4)$ alkyl; or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

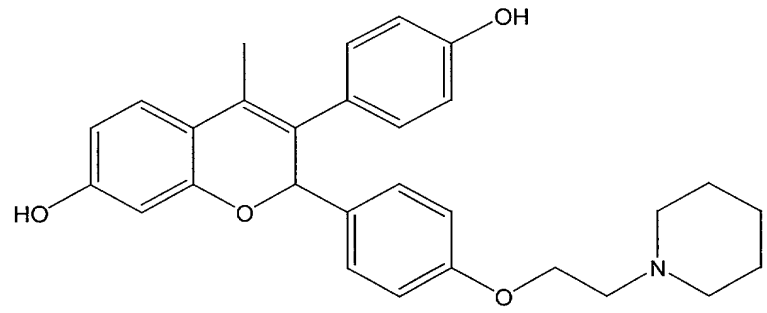
8. A method as in claim 7 wherein said estrogen agonist / antagonist is the compound, TSE-424, of formula Va below:



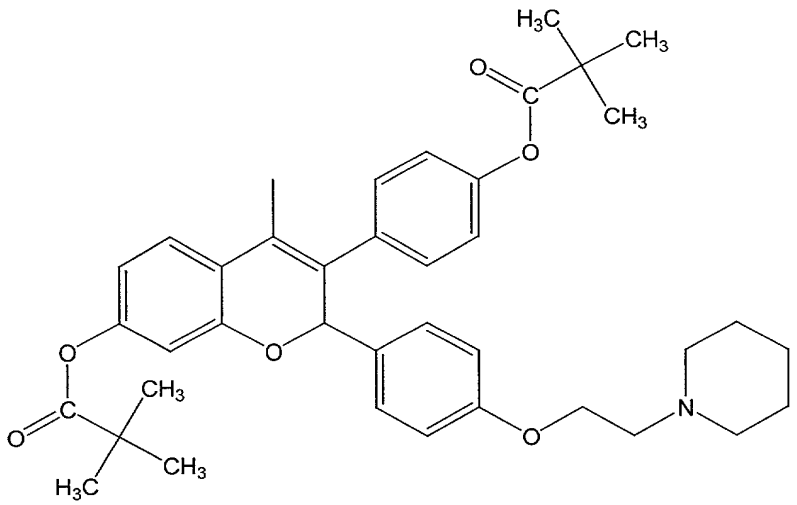

(Va)

or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

9. A use as in claim 1 wherein said estrogen agonist / antagonist is EM-652 of formula III below or is EM-800 of formula IV below:




(III)



(IV)

or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

10. A method as in claim 1 further comprising co-administrering a cyclic guanosine 3',5'-monophosphate elevator.

11. A method as in claim 8 wherein said cyclic guanosine 3',5'-monophosphate elevator is a $PDE_V$ phosphodiesterase inhibitor.

12. A method as in claim 5 further comprising co-administrering 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxy-phenyl]sufonyl]-4-methylpiperazine citrate salt.

13. A method as in claim 1 wherein said method substantially reduces the concomitant liability of adverse effects associated with estrogen administration.

14. A method as in claim 1 wherein said female sexual dysfunction is a condition selected from the group consisting of hypoactive sexual desire disorder, sexual arousal disorder, dyspareunia and vaginismus.

15. A kit for use by a consumer to treat female sexual dysfunction comprising:

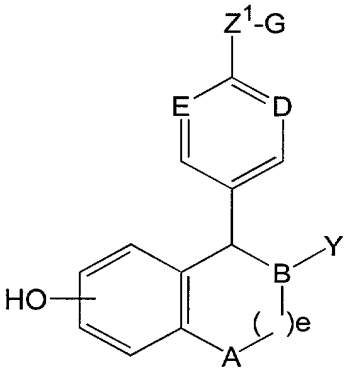
(a) a pharmaceutical composition comprising an estrogen agonist / antagonist and a pharmaceutically acceptable carrier, vehicle or diluent; and optionally,

(b) a pharmaceutical composition comprising a cyclic guanosine 3',5'-monophosphate elevator and pharmaceutically acceptable carrier, vehicle or diluent; and optionally,

(c) instructions describing a method of using the pharmaceutical composition(s) to treat female sexual dysfunction,

wherein said estrogen agonist / antagonist and said cyclic guanosine 3',5'-monophosphate elevator may optionally be combined in the same pharmaceutical composition.

16. A kit as in claim 15 wherein said estrogen agonist / antagonist of the following formula (I):




(I)

wherein:

A is selected from $CH_2$ and NR;

B, D and E are independently selected from CH and N;

Y is

(a) phenyl, optionally substituted with 1-3 substituents independently selected from $R^4$;

(b) naphthyl, optionally substituted with 1-3 substituents independently selected from $R^4$;

(c) $C_3$-$C_8$ cycloalkyl, optionally substituted with 1-2 substituents independently selected from $R^4$;

(d) $C_3$-$C_8$ cycloalkenyl, optionally substituted with 1-2 substituents independently selected from $R^4$;

(e) a five membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -$NR^2$- and -$S(O)_n$-, optionally substituted with 1-3 substituents independently selected from $R^4$;

(f) a six membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, -$NR^2$- and -$S(O)_n$- optionally substituted with 1-3 substituents independently selected from $R^4$; or

(g) a bicyclic ring system consisting of a five or six membered heterocyclic ring fused to a phenyl ring, said heterocyclic ring containing up to two heteroatoms selected from the group consisting of -O-, -$NR^2$- and -$S(O)_n$-, optionally substituted with 1-3 substituents independently selected from $R^4$;

$Z^1$ is

(a) -$(CH_2)_p$ $W(CH_2)_q$-;

(b) -$O(CH_2)_p$ $CR^5R^6$-;

(c) -$O(CH_2)_pW(CH_2)_q$-;

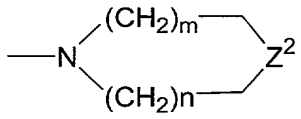
(d) -$OCHR^2CHR^3$-; or

(e) -$SCHR^2CHR^3$-;

G is

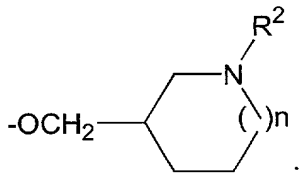
(a) -$NR^7R^8$;

(b)




wherein n is 0, 1 or 2; m is 1, 2 or 3; $Z^2$ is -NH-, -O-, -S-, or -$CH_2$-; optionally fused on adjacent carbon atoms with one or two phenyl rings and, optionally independently substituted on carbon with one to three substituents and, optionally, independently on nitrogen with a chemically suitable substituent selected from $R^4$; or

(c) a bicyclic amine containing five to twelve carbon atoms, either bridged or fused and optionally substituted with 1-3 substituents independently selected from $R^4$; or

$Z^1$ and G in combination may be  ;

W is

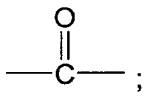
(a) $-CH_2-$;

(b) -CH=CH-;

(c) -O-;

(d) $-NR^2-$;

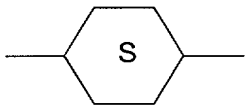
(e) $-S(O)_n-$;

(f)  ;

(g) $-CR^2(OH)-$;

(h) $-CONR^2-$;

(i) $-NR^2CO-$;

(j)  ; or

(k) $-C\equiv C-$;

R is hydrogen or $C_1$-$C_6$ alkyl;

$R^2$ and $R^3$ are independently

(a) hydrogen; or

(b) $C_1$-$C_4$ alkyl;

$R^4$ is

(a) hydrogen;

(b) halogen;

(c) $C_1$-$C_6$ alkyl;

(d) $C_1$-$C_4$ alkoxy;

(e) $C_1$-$C_4$ acyloxy;

(f) $C_1$-$C_4$ alkylthio;

(g) $C_1$-$C_4$ alkylsulfinyl;

(h) $C_1$-$C_4$ alkylsulfonyl;

(i) hydroxy ($C_1$-$C_4$)alkyl;

(j) aryl ($C_1$-$C_4$)alkyl;

(k) $-CO_2H$;

(l) -CN;

(m) -CONHOR;

(n) $-SO_2NHR$;

(o) $-NH_2$;

(p) $C_1$-$C_4$ alkylamino;

(q) $C_1$-$C_4$ dialkylamino;

(r) $-NHSO_2R$;

(s) $-NO_2$;

(t) -aryl; or

(u) -OH;

$R^5$ and $R^6$ are independently $C_1$-$C_8$ alkyl or together form a $C_3$-$C_{10}$ carbocyclic ring;

$R^7$ and $R^8$ are independently

(a) phenyl;

(b) a $C_3$-$C_{10}$ carbocyclic ring, saturated or unsaturated;

(c) a $C_3$-$C_{10}$ heterocyclic ring containing up to two heteroatoms, selected from -O-, -N- and -S-;

(d) H;

(e) $C_1$-$C_6$ alkyl; or

(f) form a 3 to 8 membered nitrogen containing ring with $R^5$ or $R^6$;

$R^7$ and $R^8$ in either linear or ring form may optionally be substituted with up to three substituents independently selected from $C_1$-$C_6$ alkyl, halogen, alkoxy, hydroxy and carboxy;

a ring formed by $R^7$ and $R^8$ may be optionally fused to a phenyl ring;

e is 0, 1 or 2;

m is 1, 2 or 3;

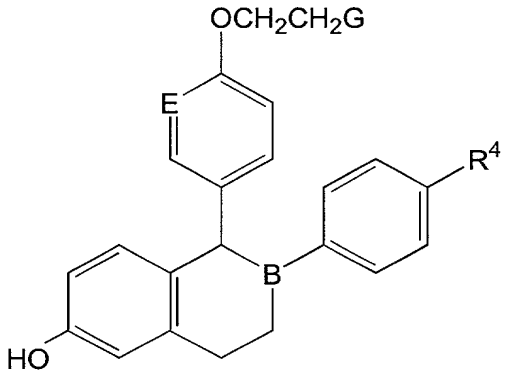
n is 0, 1 or 2;

p is 0, 1, 2 or 3;

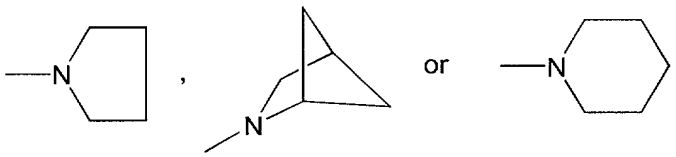
q is 0, 1, 2 or 3;

or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

17. A kit as in claim 16 wherein said estrogen agonist / antagonist is a compound of formula (IA):




(IA)

wherein G is  ;

$R^4$ is H, OH, F, or Cl; and B and E are independently selected from CH and N or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof.

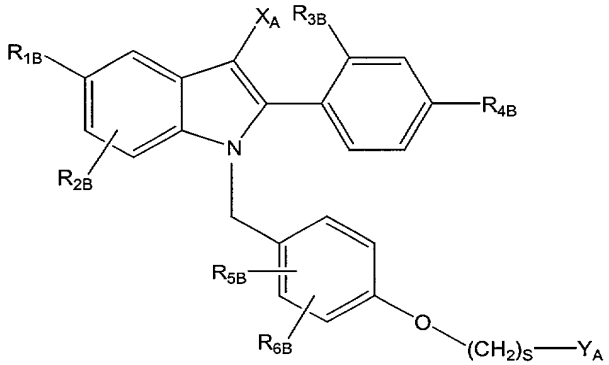
18. A kit as in claim 17 wherein said estrogen agonist / antagonist is (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof.

19. A kit as in claim 18 wherein said estrogen agonist / antagonist is in the form of a D-tartrate salt.

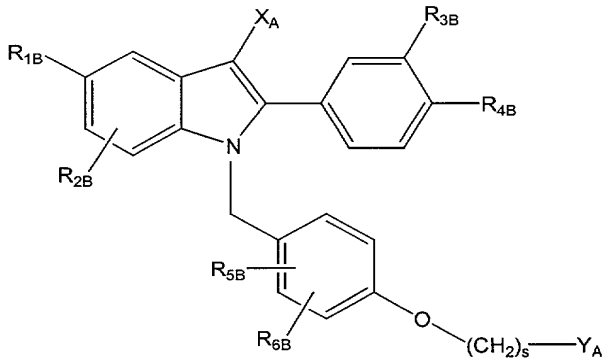
20. A kit as in claim 15 wherein said estrogen agonist / antagonist is selected from the group consisting of tamoxifen, 4-hydroxy tamoxifen, raloxifene, toremifene, centchroman, idoxifene, 6-(4-hydroxy-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-benzyl]-naphthalen-2-ol, {4-[2-(2-aza-bicyclo[2.2.1]hept-2-yl)-ethoxy]-phenyl}-[6-hydroxy-2-(4-hydroxy-phenyl)-benzo[b]thiophen-3-yl]-methanone, EM-652, EM-800, GW 5638, GW 7604 and optical or geometric isomers thereof; and pharmaceutically

acceptable salts, N-oxides, esters, quaternary ammonium salts, and prodrugs thereof.

21. A kit as in claim 15 wherein said estrogen agonist / antagonist is a compound selected from the formulas V or VI:




(V)




(VI)

wherein:

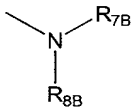
$R_{1B}$ is selected from H, OH, -O-C(O)-$C_1$-$C_{12}$ alkyl (straight chain or branched), -O-$C_1$-$C_{12}$ alkyl (straight chain or branched or cyclic), or halogens or $C_1$-$C_4$ halogenated ethers,

$R_{2B}$, $R_{3B}$, $R_{4B}$, $R_{5B}$, and $R_{6B}$ are independently selected from H, OH, -O-C(O)-$C_1$-$C_{12}$ (straight chain or branched), -O-$C_1$-$C_{12}$ (straight chain or branched or cyclic), halogens, or $C_1$-$C_4$ halogenated ethers, cyano, $C_1$-$C_6$ alkyl (straight chain or branched), or trifluoromethyl, with the proviso that, when $R_{1B}$ is H, $R_{2B}$ is not OH;

$X_A$ is selected from H, $C_1$-$C_6$ alkyl, cyano, nitro, triflouromethyl, and halogen;

s is 2 or 3;

$Y_A$ is the moiety:



wherein:

a) $R_{7B}$ and $R_{8B}$ are independently selected from the group of H, $C_1$-$C_6$ alkyl, or phenyl optionally substituted by CN, $C_1$-$C_6$ alkyl (straight chain or branched), $C_1$-$C_6$ alkoxy (straight chain or branched), halogen, -OH, $-CF_3$, or $-OCF_3$; or

b) $R_{7B}$ and $R_{8B}$ are concatenated to form a five-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, $C_1$-$C_4$ alkyl, trihalomethyl, $C_1$-$C_4$ alkoxy, trihalomethoxy, $C_1$-$C_4$ acyloxy, $C_1$-$C_4$ alkylthio, $C_1$-$C_4$ alkylsulfinyl, $C_1$-$C_4$ alkylsulfonyl, hydroxy ($C_1$-$C_4$)alkyl, $-CO_2H$, -CN-, $-CONHR_{1B}$, $-NH_2$, $-NH(C_1$-$_{C4}$ alkyl), $-N(C_1$-$C_4$ alkyl)$_2$, $-NHSO_2R_{1B}$, $-NHCOR_{1B}$, $-NO_2$, or phenyl optionally substituted with 1-3 ($C_1$-$C_4$)alkyl; or

c) $R_{7B}$ and $R_{8B}$ are concatenated to form a six-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, $C_1$-$C_4$ alkyl, trihalomethyl, $C_1$-$C_4$ alkoxy, trihalomethoxy, $C_1$-$C_4$ acyloxy, $C_1$-$C_4$ alkylthio, $C_1$-$C_4$ alkylsulfinyl, $C_1$-$C_4$ alkylsulfonyl, hydroxy ($C_1$-$C_4$)alkyl, $-CO_2H$, -CN, $-CONHR_{1B}$, $-NH_2$, $-NH(C_1$-$C_4$ alkyl), $-N(C_1$-$C_4$ alkyl)$_2$, $-NHSO_2R_{1B}$, $-NHCOR_{1B}$, $-NO_2$, or phenyl optionally substituted with 1-3 ($C_1$-$C_4$)alkyl; or

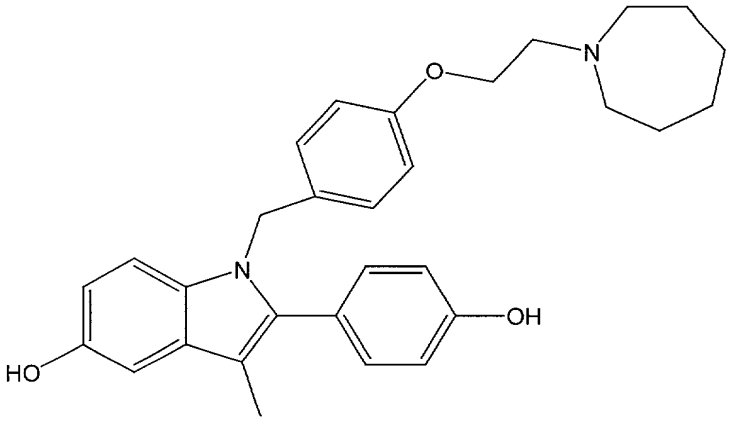
d) $R_{7B}$ and $R_{8B}$ are concatenated to form a seven-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, $C_1$-$C_4$ alkyl, trihalomethyl, $C_1$-$C_4$ alkoxy, trihalomethoxy, $C_1$-$C_4$ acyloxy, $C_1$-$C_4$ alkylthio, $C_1$-$C_4$ alkylsulfinyl, $C_1$-$C_4$ alkylsulfonyl, hydroxy ($C_1$-$C_4$)alkyl,

$-CO_2H$, -CN, $-CONHR_{1B}$, $-NH_2$, $-NH(C_1-C_4$ alkyl), $-N(C_1-C_4$ alkyl$)_2$, $-NHSO_2 R_{1B}$, $-NHCOR_{1B}$ $-NO_2$, or phenyl optionally substituted with 1-3 $(C_1-C_4)$alkyl; or

e) $R_{7B}$ and $R_{8B}$ are concatenated to form an eight-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, $C_1-C_4$ alkyl, trihalomethyl, $C_1-C_4$ alkoxy, trihalomethoxy, $C_1-C_4$ acyloxy, $C_1-C_4$ alkylthio, $C_1-C_4$ alkylsulfinyl, $C_1-C_4$ alkylsulfonyl, hydroxy $(C_1-C_4)$alkyl, $-CO_2H$, -CN, $-CONHR_{1B}$, $-NH_2$, $-NH(C_1-C_4$ alkyl), $-N(C1-C4$ alkyl$)_2$, $-NHSO_2R_{1B}$, $-NHCOR_{1B}$, $-NO_2$, or phenyl optionally substituted with 1-3 $(C_1-C_4)$alkyl; or

f) $R_{7B}$ and $R_{8B}$ are concatenated to form a saturated bicyclic heterocycle containing from 6-12 carbon atoms either bridged or fused and containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, $C_1-C_4$ alkyl, trihalomethyl, $C_1-C_4$ alkoxy, trihalomethoxy, $C_1-C_4$ acyloxy, $C_1-C_4$ alkylthio, $C_1-C_4$ alkylsulfinyl, $C_1-C_4$ alkylsulfonyl, hydroxy $(C_1-C_4)$alkyl, $-CO_2H$, -CN, $-CONHR_{1B}$, $-NH_2$, $-NH(C_1-C_4$ alkyl), $-N(C_1-C_4$ alkyl$)_2$, $-NHSO_2R_{1B}$, $-NHCOR_{1B}$, $-NO_2$, or phenyl optionally substituted with 1-3 $(C_1-C_4)$ alkyl;
or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

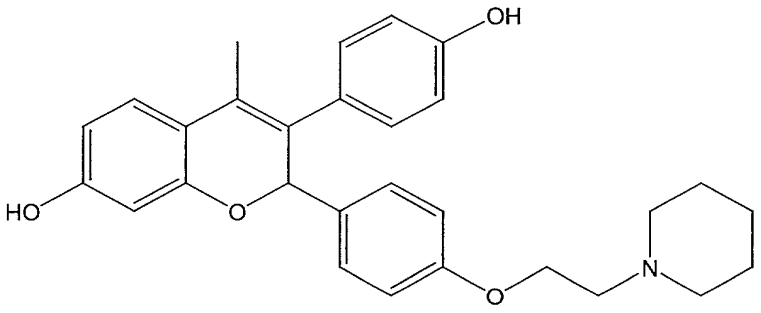
22. A kit as in claim 21 wherein said estrogen agonist / antagonist is the compound, TSE-424, of formula Va below:



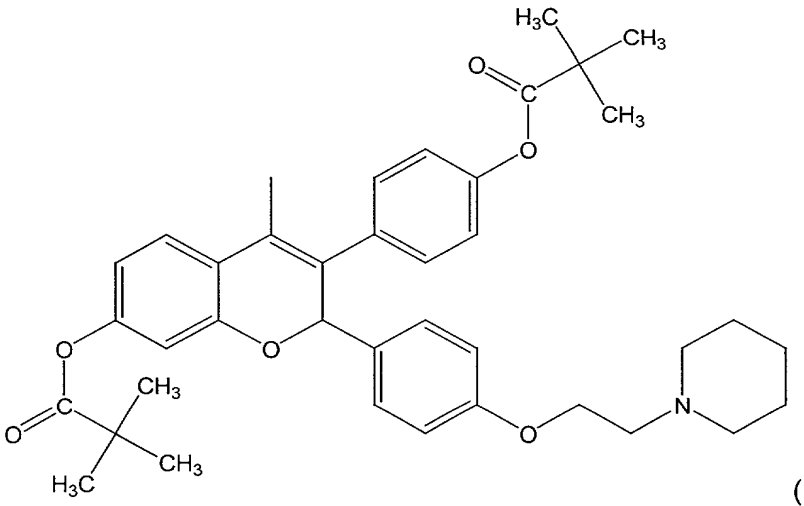

(Va)

or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

23. A kit as in claim 15 wherein said estrogen agonist / antagonist is EM-652 of formula III below or EM-800 of formula IV below:




(III)



(IV)

or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

24. A kit as in claim 15 wherein said kit further comprising a pharmaceutical composition comprising a cyclic guanosine 3',5'-monophosphate elevator and a pharmaceutically acceptable carrier, vehicle or diluent.

25. A kit as in claim 24 wherein said cyclic guanosine 3',5'-monophosphate elevator is a $PDE_V$ phosphodiesterase inhibitor.

26. A kit as in claim 25 wherein said kit further comprises a pharmaceutical composition comprising 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxy-phenyl]sufonyl]-4-methylpiperazine citrate salt and a pharmaceutically acceptable carrier, vehicle or diluent.

27. A kit as in claim 15 further comprising instructions describing a method of using the pharmaceutical composition(s) to treat female sexual dysfunction wherein said instructions indicate that the kit substantially reduces the concomitant liability of adverse effects associated with estrogen administration.

28. A kit as in claim 15 wherein said female sexual dysfunction is a condition selected from the group consisting of hypoactive sexual desire disorder, sexual arousal disorder, dyspareunia and vaginismus.

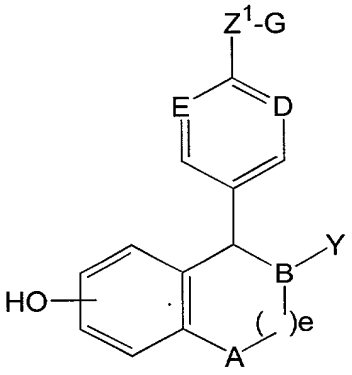
29. A pharmaceutical composition comprising:

(a) an estrogen agonist / antagonist, and

(b) a cyclic guanosine 3',5'-monophosphate elevator.

30. A pharmaceutical composition as in claim 29 wherein said cyclic guanosine 3',5'-monophosphate elevator is 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxy-phenyl]sufonyl]-4-methylpiperazine citrate salt.

31. A pharmaceutical composition as in claim 29 wherein said estrogen agonist / antagonist of the following formula (I):




(I)

wherein:

A is selected from $CH_2$ and NR;

B, D and E are independently selected from CH and N;

Y is

(a) phenyl, optionally substituted with 1-3 substituents independently selected from $R^4$;

(b) naphthyl, optionally substituted with 1-3 substituents independently selected from $R^4$;

(c) $C_3$-$C_8$ cycloalkyl, optionally substituted with 1-2 substituents independently selected from $R^4$;

(d) $C_3$-$C_8$ cycloalkenyl, optionally substituted with 1-2 substituents independently selected from $R^4$;

(e) a five membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, $-NR^2-$ and $-S(O)_n-$, optionally substituted with 1-3 substituents independently selected from $R^4$;

(f) a six membered heterocycle containing up to two heteroatoms selected from the group consisting of -O-, $-NR^2-$ and $-S(O)_n-$ optionally substituted with 1-3 substituents independently selected from $R^4$; or

(g) a bicyclic ring system consisting of a five or six membered heterocyclic ring fused to a phenyl ring, said heterocyclic ring containing up to two heteroatoms selected from the group consisting of -O-, $-NR^2-$ and $-S(O)_n-$, optionally substituted with 1-3 substituents independently selected from $R^4$;

$Z^1$ is

(a) $-(CH_2)_p W(CH_2)_q-$;

(b) $-O(CH_2)_p CR^5R^6-$;

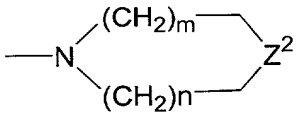
(c) $-O(CH_2)_pW(CH_2)_q-$;

(d) $-OCHR^2CHR^3-$; or

(e) $-SCHR^2CHR^3-$;

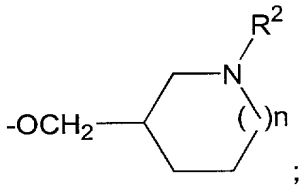
G is

(a) $-NR^7R^8$;

(b) 

wherein n is 0, 1 or 2; m is 1, 2 or 3; $Z^2$ is -NH-, -O-, -S-, or $-CH_2-$; optionally fused on adjacent carbon atoms with one or two phenyl rings and, optionally independently substituted on carbon with one to three substituents and, optionally, independently on nitrogen with a chemically suitable substituent selected from $R^4$; or

(c) a bicyclic amine containing five to twelve carbon atoms, either bridged or fused and optionally substituted with 1-3 substituents independently selected from $R^4$; or

$Z^1$ and G in combination may be  ;

W is

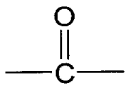
(a) $-CH_2-$;

(b) -CH=CH-;

(c) -O-;

(d) $-NR^2-$;

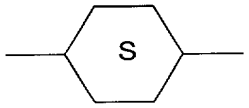
(e) $-S(O)_n-$;

(f)  ;

(g) $-CR^2(OH)-$;

(h) $-CONR^2-$;

(i) $-NR^2CO-$;

(j)  ; or

(k) $-C\equiv C-$;

R is hydrogen or $C_1$-$C_6$ alkyl;

$R^2$ and $R^3$ are independently

(a) hydrogen; or

(b) $C_1$-$C_4$ alkyl;

$R^4$ is

(a) hydrogen;

(b) halogen;

(c) $C_1$-$C_6$ alkyl;

(d) $C_1$-$C_4$ alkoxy;

(e) $C_1$-$C_4$ acyloxy;

(f) $C_1$-$C_4$ alkylthio;

(g) $C_1$-$C_4$ alkylsulfinyl;

(h) $C_1$-$C_4$ alkylsulfonyl;

(i) hydroxy ($C_1$-$C_4$)alkyl;

(j) aryl ($C_1$-$C_4$)alkyl;

(k) $-CO_2H$;

(l) -CN;

(m) -CONHOR;

(n) $-SO_2NHR$;

(o) $-NH_2$;

(p) $C_1$-$C_4$ alkylamino;

(q) $C_1$-$C_4$ dialkylamino;

(r) $-NHSO_2R$;

(s) $-NO_2$;

(t) -aryl; or

(u) -OH;

$R^5$ and $R^6$ are independently $C_1$-$C_8$ alkyl or together form a $C_3$-$C_{10}$ carbocyclic ring;

$R^7$ and $R^8$ are independently

(a) phenyl;

(b) a $C_3$-$C_{10}$ carbocyclic ring, saturated or unsaturated;

(c) a $C_3$-$C_{10}$ heterocyclic ring containing up to two heteroatoms, selected from -O-, -N- and -S-;

(d) H;

(e) $C_1$-$C_6$ alkyl; or

(f) form a 3 to 8 membered nitrogen containing ring with $R^5$ or $R^6$;

$R^7$ and $R^8$ in either linear or ring form may optionally be substituted with up to three substituents independently selected from $C_1$-$C_6$ alkyl, halogen, alkoxy, hydroxy and carboxy;

a ring formed by $R^7$ and $R^8$ may be optionally fused to a phenyl ring;

e is 0, 1 or 2;

m is 1, 2 or 3;

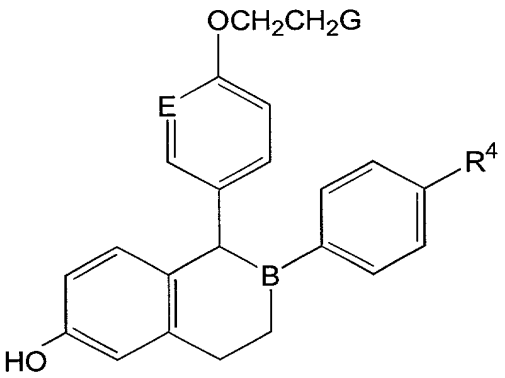
n is 0, 1 or 2;

p is 0, 1, 2 or 3;

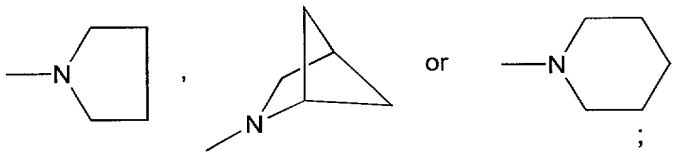
q is 0, 1, 2 or 3;

or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

32. A pharmaceutical composition as in claim 31 wherein said estrogen agonist / antagonist is a compound of formula (IA):




(IA)

wherein G is 

;

$R^4$ is H, OH, F, or Cl; and B and E are independently selected from CH and N or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof.

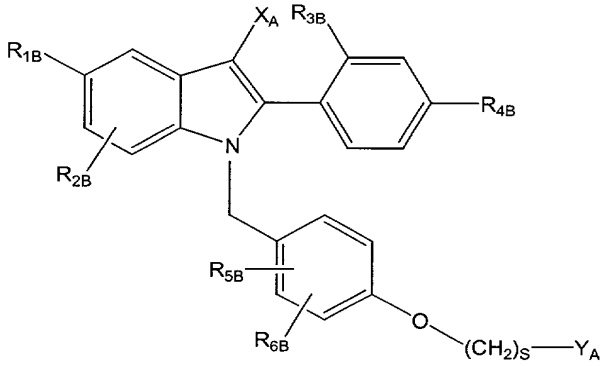
33. A pharmaceutical composition as in claim 32 wherein said estrogen agonist / antagonist is (-)-cis-6-phenyl-5-[4-(2-pyrrolidin-1-yl-ethoxy)-phenyl]-5,6,7,8-tetrahydro-naphthalene-2-ol or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt, or a prodrug thereof.

34. A pharmaceutical composition as in 33 wherein said estrogen agonist / antagonist is in the form of a D-tartrate salt.

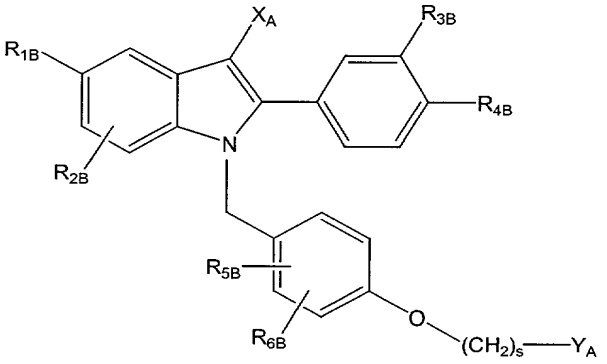
35. A pharmaceutical composition as in claim 29 wherein said estrogen agonist / antagonist is selected from the group consisting of tamoxifen, 4-hydroxy tamoxifen, raloxifene, toremifene, centchroman, idoxifene, 6-(4-hydroxy-phenyl)-5-[4-(2-piperidin-1-yl-ethoxy)-benzyl]-naphthalen-2-ol, {4-[2-(2-aza-bicyclo[2.2.1]hept-2-yl)-

ethoxy]-phenyl}-[6-hydroxy-2-(4-hydroxy-phenyl)-benzo[b]thiophen-3-yl]-methanone, EM-652, EM-800, GW 5638, GW 7604 and optical or geometric isomers thereof; and pharmaceutically acceptable salts, N-oxides, esters, quaternary ammonium salts, and prodrugs thereof.

36. A pharmaceutical composition as in claim 29 wherein said estrogen agonist / antagonist is a compound selected from the formulas V or VI:




(V)




(VI)

wherein:

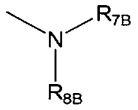
$R_{1B}$ is selected from H, OH, -O-C(O)-$C_1$-$C_{12}$ alkyl (straight chain or branched), -O-$C_1$-$C_{12}$ alkyl (straight chain or branched or cyclic), or halogens or $C_1$-$C_4$ halogenated ethers,

$R_{2B}$, $R_{3B}$, $R_{4B}$, $R_{5B}$, and $R_{6B}$ are independently selected from H, OH, -O-C(O)-$C_1$-$C_{12}$ (straight chain or branched), -O-$C_1$-$C_{12}$ (straight chain or branched or cyclic), halogens, or $C_1$-$C_4$ halogenated ethers, cyano, $C_1$-$C_6$ alkyl (straight chain or branched), or trifluoromethyl, with the proviso that, when $R_{1B}$ is H, $R_{2B}$ is not OH;

$X_A$ is selected from H, $C_1$-$C_6$ alkyl, cyano, nitro, triflouromethyl, and halogen;

s is 2 or 3;

$Y_A$ is the moiety:




wherein:

a) $R_{7B}$ and $R_{8B}$ are independently selected from the group of H, $C_1$-$C_6$ alkyl, or phenyl optionally substituted by CN, $C_1$-$C_6$ alkyl (straight chain or branched), $C_1$-$C_6$ alkoxy (straight chain or branched), halogen, -OH, -$CF_3$, or -$OCF_3$; or

b) $R_{7B}$ and $R_{8B}$ are concatenated to form a five-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, $C_1$-$C_4$ alkyl, trihalomethyl, $C_1$-$C_4$ alkoxy, trihalomethoxy, $C_1$-$C_4$ acyloxy, $C_1$-$C_4$ alkylthio, $C_1$-$C_4$ alkylsulfinyl, $C_1$-$C_4$ alkylsulfonyl, hydroxy ($C_1$-$C_4$)alkyl, -$CO_2$H, -CN-, -$CONHR_{1B}$, -$NH_2$, -NH($C_1$-$C_4$ alkyl), -N($C_1$-$C_4$ alkyl)$_2$, -$NHSO_2R_{1B}$, -$NHCOR_{1B}$, -$NO_2$, or phenyl optionally substituted with 1-3 ($C_1$-$C_4$)alkyl; or

c) $R_{7B}$ and $R_{8B}$ are concatenated to form a six-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, $C_1$-$C_4$ alkyl, trihalomethyl, $C_1$-$C_4$ alkoxy, trihalomethoxy, $C_1$-$C_4$ acyloxy, $C_1$-$C_4$ alkylthio, $C_1$-$C_4$ alkylsulfinyl, $C_1$-$C_4$ alkylsulfonyl, hydroxy ($C_1$-$C_4$)alkyl, -$CO_2$H, -CN, -$CONHR_{1B}$, -$NH_2$, -NH($C_1$-$C_4$ alkyl), -N($C_1$-$C_4$ alkyl)$_2$, -$NHSO_2R_{1B}$, -$NHCOR_{1B}$, -$NO_2$, or phenyl optionally substituted with 1-3 ($C_1$-$C_4$)alkyl; or

d) $R_{7B}$ and $R_{8B}$ are concatenated to form a seven-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, $C_1$-$C_4$ alkyl, trihalomethyl, $C_1$-$C_4$ alkoxy, trihalomethoxy, $C_1$-$C_4$ acyloxy, $C_1$-$C_4$ alkylthio, $C_1$-$C_4$ alkylsulfinyl, $C_1$-$C_4$ alkylsulfonyl, hydroxy ($C_1$-$C_4$)alkyl, $-CO_2H$, -CN, $-CONHR_{1B}$, $-NH_2$, $-NH(C_1$-$C_4$ alkyl), $-N(C_1$-$C_4$ alkyl)$_2$, $-NHSO_2R_{1B}$, $-NHCOR_{1B}$ $-NO_2$, or phenyl optionally substituted with 1-3 ($C_1$-$C_4$)alkyl; or

e) $R_{7B}$ and $R_{8B}$ are concatenated to form an eight-membered saturated heterocycle containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, $C_1$-$C_4$ alkyl, trihalomethyl, $C_1$-$C_4$ alkoxy, trihalomethoxy, $C_1$-$C_4$ acyloxy, $C_1$-$C_4$ alkylthio, $C_1$-$C_4$ alkylsulfinyl, $C_1$-$C_4$ alkylsulfonyl, hydroxy ($C_1$-$C_4$)alkyl, $-CO_2H$, -CN, $-CONHR_{1B}$, $-NH_2$, $-NH(C_1$-$C_4$ alkyl), $-N(C1$-$C4$ alkyl)$_2$, $-NHSO_2R_{1B}$, $-NHCOR_{1B}$, $-NO_2$, or phenyl optionally substituted with 1-3 ($C_1$-$C_4$)alkyl; or

f) $R_{7B}$ and $R_{8B}$ are concatenated to form a saturated bicyclic heterocycle containing from 6-12 carbon atoms either bridged or fused and containing one nitrogen heteroatom, the heterocycle being optionally substituted with 1-3 substituents independently selected from the group consisting of hydrogen, hydroxyl, halo, $C_1$-$C_4$ alkyl, trihalomethyl, $C_1$-$C_4$ alkoxy, trihalomethoxy, $C_1$-$C_4$ acyloxy, $C_1$-$C_4$ alkylthio, $C_1$-$C_4$ alkylsulfinyl, $C_1$-$C_4$ alkylsulfonyl, hydroxy ($C_1$ -$C_4$)alkyl, $-CO_2$ H, -CN, - $CONHR_{1B}$, $-NH_2$, $-NH(C_1$-$C_4$ alkyl), $-N(C_1$-$C_4$ alkyl)$_2$, $-NHSO_2R_{1B}$, $-NHCOR_{1B}$, $-NO_2$, or phenyl optionally substituted with 1-3 ($C_1$-$C_4$) alkyl;
or an optical or geometric isomer thereof; or a pharmaceutically acceptable salt, N-oxide, ester, quaternary ammonium salt or prodrug thereof.

32. A pharmaceutical composition as in claim 25 further comprising a pharmaceutical composition comprising a cyclic guanosine 3',5'-monophosphate elevator.

33. A pharmaceutical composition as in claim 31 wherein said cyclic guanosine 3',5'-monophosphate elevator is a $PDE_V$ phosphodiesterase inhibitor.

34. A pharmaceutical composition as in claim 29 further comprising a pharmaceutical composition comprising 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxy-phenyl]sufonyl]-4-methylpiperazine citrate salt.